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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			ZARA, JANE J	
			ART UNIT	PAPER NUMBER
			1635	29

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.
09/068,751

Applicant(s)
Franz et al

Examiner
Jane Zara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Aug 8, 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 83-120 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 83-120 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☒ Other: sequence compliance

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DETAILED ACTION

This Office action is in response to the communications filed August 8, 2002, Paper Nos. 27 and 28.

Claims 83-120 are pending in the instant application.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8-8-03 has been entered.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **No paper or computer disc copies of the nucleotide sequences have been provided for the sequences**

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disclosed in the specification (e.g. see SEQ ID NO: 1 in Annex I and the claims). See the accompanying Notice to Comply.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 83, 84, 88-92, 95-120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 83 and 91, it is unclear whether the multiple ITR sequences, and whether the packaging signal, are each obtained from a single virus, or from different viral sources.

Appropriate clarification is requested.

In claims 83 and 91, it is unclear whether the ITR and packaging signal are located 5' or 3' to the promoter fragments.

In claim 83, line 10 and in claim 91, line 22, it is unclear what “the nucleic acid sequence to be expressed” is referring to (e.g. this sequence was not previously described in the claim).

In claim 84, line 3, nucleotide residues are described, but it is unclear which nucleotide sequence (e.g. which SEQ ID NO.) these nucleotide residues are referring to (e.g. perhaps indicating a SEQ ID NO. for the MLC2 gene would be remedial).

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In claim 85, line 4, the abbreviations "m.u." and "Ad5" are vague and unclear (e.g. perhaps spelling out the full names of these abbreviations would be remedial).

In claims 89, 90, 96 and 97, lines 2-3, the phrase "proteinaceous gene product" is vague and unclear. Appropriate clarification is requested (e.g. perhaps replacing this phrase with -- protein-- would be remedial).

In claim 92, line 1, the abbreviation "CSS" is vague and unclear. Appropriate clarification is requested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 83, 84, 86- rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Specification Objection and Claim Rejections - 35 USC § 112

This application does not comply with the rules for the deposit of biological material as set forth below in the Suggestion for Deposit of Biological Material. For ATCC deposits, please be sure to use the current address in Virginia, rather than the former address in Maryland.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 USC § 112, first paragraph as failing to provide an enabling disclosure for the claimed invention.

Claim 85 is rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

It is apparent that the vector pADRSV β -gal is required to practice the claimed invention. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If this is not so obtainable or available, the enablement requirements of 35 USC § 112, first paragraph, may be satisfied by a deposit of pADRSV β -gal. A suggestion for deposit of biological materials is provided below.

The vector pADRSV β -gal is required material as a claimed invention. The specification does not provide a repeatable method for obtaining the vector pADRSV β -gal, and it does not appear to be a readily available material. Deposit of the vector pADRSV β -gal would satisfy the enablement requirements of 35 USC § 112. A suggestion for deposit of biological materials is provided:

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A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Se 37 CFR 1.801 through 1.809. Such a declaration:

1. Identifies declarant.
2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.
3. States that the deposited material has been accorded a specific (recited) accession number.
4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent.
5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to tone determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122.
6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer.
7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine of imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocable removed upon the granting of a patent.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 83, 84, 86-89, 104, 105, 110, 111, 116 and 117 are rejected under 35 U.S.C.

102(a) as being anticipated by Rothmann et al.

Rothmann et al teach compositions and methods of cardiac delivery comprising the administration of a replication defective, recombinant adenoviral vector and pharmaceutically acceptable carrier to the cardiac tissue or heart cavity of a subject, which vector comprises two inverted terminal repeats and a packaging signal of the adenovirus, and further comprises a mammalian myosin light chain-2 (MLC-2) promoter, and a nucleic acid encoding beta-galactosidase, operatively linked to the MLC-2 promoter, and which promoter is effective for cardiac tissue specific expression of the operatively linked galactosidase (See abstract on page 919; figure 1 and text on page 920-921; figure 2 on page 922; figures 3 and 4 on page 923; text on page 924).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 83, 84, 86-90, 98-100, 104-106, 110-112 and 116-118 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rothmann et al as applied to claims 83, 84, 86-89, 104, 105, 110, 111, 116 and 117 above, and further in view of Sukhatme.

The claims are drawn to compositions and methods comprising the in vivo administration of a replication defective, recombinant adenoviral vector and pharmaceutically acceptable carrier to the cardiac tissue or heart cavity of a subject, which vector comprises two inverted terminal repeats and a packaging signal of the adenovirus, and further comprises a mammalian myosin light chain-2 (MLC-2) promoter, and a nucleic acid encoding nitric oxide synthetase, operatively linked to the MLC-2 promoter, and which promoter is effective for cardiac tissue specific expression of the operatively linked nucleic acid encoding nitric oxide synthetase.

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Rothmann et al teach compositions and methods of cardiac delivery comprising the administration of a replication defective, recombinant adenoviral vector and pharmaceutically acceptable carrier to the cardiac tissue or heart cavity of a subject, which vector comprises two inverted terminal repeats and a packaging signal of the adenovirus, and further comprises a mammalian myosin light chain-2 (MLC-2) promoter, and a nucleic acid encoding a protein, operatively linked to the MLC-2 promoter, and which promoter is effective for cardiac tissue specific expression of the operatively linked nucleic acid encoding a protein (See abstract on page 919; figure 1 and text on page 920-921; figure 2 on page 922; figures 3 and 4 on page 923; text on page 924).

Rothmann et al do not teach the administration of the recombinant, replication deficient adenoviral vector comprising an operatively linked nucleic acid encoding nitric oxide synthetase, nor the transfection of target cells comprising a composition further comprising liposomes.

Sukhatme teaches the in vitro and in vivo administration of compositions comprising replication defective, recombinant adenoviral vector, a pharmaceutically acceptable carrier, and liposomes, and which vector comprises a nucleic acid encoding nitric oxide synthetase operatively linked to a promoter appropriate for its expression in a target cell upon delivery (See especially col. 1, line 26-col. 2, line 7; col. 6, lines 3-56; col. 12, lines 51-56).

It would have been obvious to one of ordinary skill in the art to utilize a recombinant, replication deficient adenoviral vector comprising an operatively linked nucleic acid encoding nitric oxide synthetase because Sukhatme teaches the utilization of such vectors for target cell

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transfection, delivery and expression of nitric oxide synthetase. One of ordinary skill in the art would have been motivated to transfect appropriate target cells using recombinant adenoviral vectors because both Rothmann et al and Sukhatme teach successful target cell delivery and recombinant gene expression in appropriate target cells in vivo and in vitro using adenoviral vectors comprising nucleic acids operatively linked to appropriate promoters for target cell expression, and Sukhatme teaches nitric oxide synthetase expression in target cells using adenoviral vectors in compositions further comprising liposomes. One of ordinary skill in the art would have been motivated to transfect and appropriately express nitric oxide synthetase in target cells because Sukhatme teaches the transfection of a nucleic acid encoding this polypeptide in target cells in order to prevent allograft rejection in areas of organ transplant. One of ordinary skill in the art would have expected that transfection of nucleic acids encoding proteins would be appropriately delivered and expressed using adenoviral vectors in combination with liposomes because Sukhatme teaches transfection and delivery to appropriate target cells using these compositions.


Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

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Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is (703) 306-5820. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.


RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

JZ

October 26, 2003